IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of: Ayres

Art Unit: 1615

Application No. 09/887,318

Filed: June 21, 2001

For: A COATED, PLATFORM-GENERATING TABLET

Examiner: Simon J. Oh

Date: July 11, 2003

**CERTIFICATE OF MAILING**

I hereby certify that this paper and the documents referred to as being attached or enclosed herewith are being deposited with the United States Postal Service on 7-14-03 as First Class Mail in an envelope addressed to: MAIL STOP AF, COMMISSIONER FOR PATENTS, P.O. BOX 1450, ALEXANDRIA, VA 22313-1450.

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**DECLARATION BY LINNA R. CHEN, Ph.D. PURSUANT TO 37 C.F.R. § 1.132**

I, Linna R. Chen, hereby declare as follows:

1. A copy of my *curriculum vitae* is attached hereto (Exhibit B).

2. I understand that claims 1–34, 58, 59, 63, 73, 79, 80 and 82–90 of the referenced application are rejected under 35 U.S.C. § 103(a) as allegedly being obvious over U.S. Patent No. 6,183,780 to Van Balken et al. (Van Balken) in view of U.S. Patent No. 6,120,803 to Wong et al. (Wong).

3. I have read and understood the specification and claims of U.S. patent application No. 09/887,318 and the Office action dated June 3, 2003. I also have reviewed Van Balken and Wong as cited by the Examiner against this application.

4. In paragraph 3, on page 5, the Office action appears to contend that a combination of Van Balken's coating with Wong's swellable core material would provide a tablet exhibiting a sustained release profile after a pre-determined lag time. However, Van Balken's coating in combination with a swellable core composition, with or without Wong's circumscribing band,

would not yield a sustained release profile after a pre-determined lag time. Indeed, Van Balken expressly states that such a combination will not work to provide the release profile suggested by the Office action. For example, at column 1, lines 46–63, Van Balken describes the disadvantages of tablets having a "swellable core and an outer membrane of water-insoluble material." Specifically Van Balken states that such formulations are "not suitable for obtaining a pulsatile release in combination with a longer (6 to 14 hours) lag-time." Moreover, Van Balken states that "the variation in lag-time is unpredictable." Thus, Van Balken teaches that use of a swellable core unpredictably affects lag time, and accordingly at column 3, lines 39–45, Van Balken states that the composition is chosen in such a way that "the composition of the carrier has no influence on the lag-time of the system." Therefore, Van Balken's coating is unsuitable for providing delayed release after a predetermined lag time when used to coat a swellable core, such as the core materials disclosed by Wong. Thus, the Office action's allegation that such a combination would provide sustained release after a pre-determined lag time is incorrect.

5. The Office action cites, at page 5, Van Balken's text at column 5, lines 8–13, for teaching that "sustained-release of a drug is desirable after a predetermined lag time." This reading of Van Balken is incorrect. Van Balken's formulations are solely directed to immediate release compositions. The bulk of Van Balken's text from column 4, line 54 through column 5, line 13, explains how prior art coatings, such as those disclosed in U.S. Patent No. 4,798,724 and EP 0655 240, which respectively disclose water soluble and water erodable coating materials, are unsuitable for Van Balken's formulations. In the cited section, Van Balken teaches that delayed immediate release is desired, and that the water-soluble coating materials would provide a different release profile, such as sustained release, and are therefore unsuitable. Specifically, Van Balken states at column 4, lines 60–62, that "to prevent release of active substance from the formulation by means of diffusion o[r] permeation, the coating should not comprise substantial amounts of polymeric coating materials that are soluble and/or erodable." Rather than using such water soluble coating materials, Van Balken uses "water-insoluble coating materials." See, column 4, line 20 (emphasis added). In contrast, claim 1 of the present application features a coating comprising a "water-soluble modifier." Thus, Van Balken expressly states that the coating materials claimed in the current application, which comprise water-soluble modifiers, are unsuitable for his purposes.

Van Balken further discusses other dosage forms that exhibit release via diffusion or permeation rather than Van Balken's desired immediate release profile. For example, at column 5, lines 4–7, Van Balken describes EP 0 655 240 as having a coating that is "eroded, leading to an increasing permeability and consequently diffusion of the active substance through the coating." In contrast, when Van Balken's coating is exposed to gastrointestinal fluids as described at column 4, lines 52 and 53, "[o]nly the plasticizer leaks away from the coating." Thus, the Office action has misconstrued Van Balken's text as teaching that sustained release of a drug is desirable. Van Balken actually teaches that sustained release, as apparently would be provided by the coating of EP 0 655 240, should be avoided.

6. At page 3 the Office action cites Van Balken's description of his core material at column 3, lines 32–45, as including "a small amount of a swellable material." However, this statement is taken out of context. The Office action ignores the language at column 3, lines 39–43, which states that the composition is chosen in such a way that "an immediate release carrier, having no substantial swelling properties is obtained, which means that the composition of the carrier has no influence on the lag-time of the system." (Emphasis added) Thus the core composition as a whole does not swell, despite including a "small amount" of a swellable material. Indeed, at column 3, lines 23–25, Van Balken distinguishes the prior art in that "the core of the present invention does not have swelling properties." Van Balken's core does not swell. In contrast, rupture of the coating in the presently claimed tablets occurs due to swelling of the tablet contents. See, for example, page 17, lines 13–20, of the present application as filed, which explains that "after sufficient swelling occurs, the polymer film coating ruptures."

7. The Office action argues that swelling is not required for gastric retention and that Wong provides for more than one method for gastric retention. Specifically, the Office action states at lines 2–3, on page 6, that "[t]he disclosed dosage form may comprise a gastric-emptying delaying agent to facilitate retention in stomach." However, a gastric-emptying delaying agent is only intended as an optional feature in addition to a swellable core when the dosage form is administered to a subject in the fasted state to delay gastric emptying. For example, Wong defines his dosage form, in the abstract at lines 4–6, stating that "[t]he active agent dosage form is a polymer matrix that swells upon contact with the fluids of the stomach." (Emphasis added).

Wong discusses gastric-emptying delaying agents "[t]o facilitate retention of the dosage forms of the invention, particularly if the dosage form is to be administered to a subject in the fasted state, it may be desirable to combine one or more gastric-emptying delaying agents with the active agent composition containing a gastric-emptying delaying agent." Column 15, lines 61–66, (emphasis added). Thus, an addition of a gastric-emptying delaying agent is only a feature secondary to the swellable core to delay gastric emptying for Wong's dosage form. Swelling in stomach is still needed for gastric retention, no matter whether a gastric-emptying delaying agent is present or not.

8. I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under 18 U.S.C. 1001 and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

By Linna R. Chen
Linna R. Chen, Ph.D.

Date 7/11/2003

# *Curriculum Vitae*

## *Linna R. Chen, Ph.D.*

Address: 3355 Crescent Dr.
West Linn, OR 97068

**Education**

Ph.D., Pharmaceutics, University of Minnesota (1999)

Title: Solid-State Behavior of Pharmaceutical Hydrates

Advisor: David J.W. Grant, Ph.D., Dr. Sc.

Committee Members: Theodore P. Labuza, Ph.D.; Eric Munson, Ph.D.; Timothy Wiedmann, Ph.D.; David J.W. Grant, Ph.D., Dr. Sc.

B.S., Pharmacy, Purdue University (1992)

**Expertise**

Pharmaceutical Dosage Formulation; Crystal Polymorphism; Drug-Moisture Interaction; Dehydration and Hydration Kinetics; Computer Modeling of Quantitative Molecular Structure and Physical Property Relationships.

**Working Experience**

2001–2002. Senior Scientist. Department of Candidate Enabling and Development. Pfizer Pharmaceutical R & D, Ann Arbor, Michigan.

1999–2001. Scientist. Department of Lead Optimization. Pfizer Pharmaceutical R & D, Ann Arbor, Michigan.

1994 –1998. Graduate Research. Supervisor: Dr. David Grant, Department of Pharmaceutics, University of Minnesota, Minneapolis, Minnesota.

1989. Undergraduate Research: Synthesizing anti-HIV drug (drug that intercalates into viral RNA or DNA). Supervisor: Dr. Stephen Byrn, Department of Medicinal Chemistry, School of Pharmacy, Purdue University, West Lafayette, Indiana.

**Professional Activities**

- Member of the American Association of the Pharmaceutical Scientists (AAPS).
- Member of the 28th Annual Pharmaceutics Graduate Student Meeting Organization Committee, Minneapolis, Minnesota, 1996.
- Member of the AAPS short course planning committee, 2002.

**Publications**

- Nuclear magnetic resonance and infrared spectroscopic analysis of nedocromil hydrates. *Pharm. Res.* **2000**, *17(5)*, 619-624.
- Solid-state behavior of cromolyn sodium hydrates. *J. Pharm. Sci.* **1999**, *88(11)*, 1191-1200.
- Extension of Clausius-Clapeyron equation to predict hydrate stability at different temperatures. *Pharm. Dev. Technol.* **1998**, *3(4)*, 487-494.

- Physical Characterization of Nedocromil Sodium Hydrates. *J. Pharm. Sci.* **1998**, *87(9),* 1052-1061.
- Dissolution behavior of a poorly water-soluble compound in the presence of Tween 80. *Pharm. Res.***2003** *20(5)*, 797-801.
- Structural and physicochemical characterization of new methanol + water mixed solvate of nedocromil sodium. To be submitted to *J. Chem. Crystallogr.*
- Dehydration kinetics of nedocromil sodium trihydrate. To be submitted to *Pharm. Res.*

**Presentations**

- L. Chen, V. Young, B.E. Padden, E.J. Munson, and D.J.W. Grant. Structural and Physicochemical characterization of a new mixed methanol + water solvate of nedocromil sodium. *Pharm. Res.* 1997, 14, S-202.
- L. Chen and D.J.W. Grant. Extension of the Clausius-Clapeyron equation to predict the water activity range for hydrate stability at different temperatures. *Pharm. Res.* 1996, 13, S-340.
- L. Chen and D.J.W. Grant. Effect of water vapor pressure on the dehydration kinetics of nedocromil sodium trihydrate. *Pharm. Res.* 1996, 13, S-356.